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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,860	01/07/2002	Jose R. F. Corvalan	ABGENIX.051A	5403

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GEORGE YAHWAK ESQ.
555 LONG WHARF DRIVE, 9TH FLOOR
NEW HAVEN, CT 06511

EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/041,860	Applicant(s) CORVALAN ET AL.	
	Examiner Phuong Huynh	Art Unit 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 May 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *02 June 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *2,23,33 and 44*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1,22,24-32,34-43 and 45*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See coninutation of 11.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

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Continuation of 5: Applicant's reply has overcome the following rejection(s): The proposed amendment filed 5/4/05 has overcome the objection of claims 2, 23, 33 and 44 and the objection of the specification.

Contiunation of 11:

Claims 1, 22, 24-32, 34-43 and 45 stand rejected under 35 U.S.C. 112, first paragraph, for enablement and written description for the same reasons of record.

Applicants' arguments filed 5/4/05 have been fully considered but are not found persuasive. Applicants' position is that antibodies to PDGFD are enabled. Although applicants agree that the antibodies of the present invention include antibodies that bind non-human PDGFD, applicants strongly disagree with the Examiner's contention. Applicants provide the attached reference, Ostendorf, T. et al tQA Fully Human Monoclonal Antibody (CR002) Ident6es PDGF-D as a Novel Mediator of Mesangioprolferative Glomerulonephritis", J Am Soc Nephrol 14:2237-2247, 2003 ("Ostendorf" Exhibit A) in which it is shown that CR002.6.4 (which is Cur 2-6.4 of the current invention) binds specifically to human, murine and rat PDGFDD (DD meaning homodimer of PDGFD), see page 2242-2243 and Figure 4. The present specification therefore provides at least one specific embodiment with specificity to PDGFD, broader than merely human PDGFD, clearly enabling the claimed invention. Applicants respectfully submit that a person skilled in the art can clearly obtain guidance with respect to the structure of the light chain from the specification (page 9). For example, the specification specifically provides: 1) light chain germline sequences (see page 62, lines 18-2 and page 64, lines 1-24); 2) specific light chain sequences (Figures 3-21, nucleic acid sequences SEQ m NOs: 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 81, 83, 85, 87, 89, 91, amino acid sequence SEQ ID NOs:14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 39, 41, 43, 45, 47, 49 and Figure 49); and 3) specific light chain CDR sequences for a human monoclonal antibody that binds to PDGFD (see Figure 49). The instant application specifically teaches that VH1-8 derived sequences can be combined with sequences derived from light chain germline sequences A19 (Antibody 1.49); A20 (Antibody 1.45); A27 (Antibody 6.4); and A30 (antibodies 1.19, 1.18 and 1.46). More specifically, for example, the specification teaches that light chain SEQ ID NO: 49 can be paired with the heavy chain of SEQ ID NO: 48, see Example 7 beginning at page 56 and Figure 21.

Applicants respectfully submit that V D J genes for antibodies specific for PDGFD are enabled: Applicants need not provide the nucleotide sequence of human VH1-8, JH6B and D5-18, for the present invention to be enabled as this information is readily available in the public domain and one of skill in the art would know how to obtain such information. Furthennore, one of skill in the art would be able to

obtain any needed information regarding introns, exons and promoter regions from the public domain. Homologs of human VH1-8, JH6B and D5-18 genes in other species are not within the scope of human monoclonal antibodies of the invention. Furthermore, as stated above, the antibodies of the invention do bind to PDGFD other than human PDGFD. The scope of claims 22, 23 and dependent claims 24-31, claims 32, 33 and dependent claims 34-39, 41, claims 42, 44 and dependent claim 45 encompasses antibodies at specifically bind to PDGFD, wherein such antibodies are encoded by human VH1-8 and JH6B and is fully enabled by the present specification as filed. The Examiner seems to contend that providing the nucleotide sequence of human VH1-8 family gene, a JH6B family gene and a human D5-18 family gene is necessary to avoid unpredictability of which V D J sequences combine to provide a human antibody that binds to PDGFD. The present specification provides extensive specific examples for the following examples of V D J combinations which provide human antibodies specific to PDGFD:
VH1-8 with 172 and JH6b (exemplified by Antibodies 1.40.1 and 1.46.1);
VH1-8 with D3-16 and JH6b (exemplified by Antibody 1.19.1);
VH1-8 with D5-12 and JH6b (exemplified by Antibody 1.49.1);
VH1-8 with D5-18 and JH6b (exemplified by Antibody 6.4.1);
VH1-8 with D6-19 and JH6b (exemplified by Antibody 1.18);
VH1-8 with DK4 and JH6b (exemplified by Antibody 1.45);
VH1-18 with D21-9 and JH6b (exemplified by Antibody 1.33);
VH1.-18 with D21-9 and JH4b (exemplified by Antibody 1.48.1);
VH3-21 with D3-16 and JH4b (exemplified by Antibody 1.6.1);
V1-13-33 with D21-9 and JH6b (exemplified by Antibody 1.38.1);
V143-33 with D5-18 and JH6b (exemplified by Antibodies 1.17.1 and 1.24.1);
V1-13-53 with D4-17 and JH6b (exemplified by Antibody 1.11.1);
VH5-51 with D3-10 and JH4b (exemplified by Antibodies 1.23.1, 1.25.1 and 1.39.1);
VH5-51 with D3-16 and JH5b (exemplified by Antibody 1.51.1); and
VH5-51 with D5-12 and JH6b (exemplified by Antibody 1.29). See, for example, Figure 22A. Applicants have provided 7 antibodies that are encoded by or derived from VH1-8; 2 antibodies from VH1-18; l antibody from VH3-21; 3 antibodies from VH3-33; and 5 antibodies from VH5-51; all of which bind to PDGFD. Two antibodies are provided that are encoded by or derived from D2; 3 antibodies from D21-9; 3 antibodies from D3-10; 3 antibodies from D3-16; 1 antibody from D4-17; 2 antibodies from D5-12; 3 antibodies from D5-18; 1 antibody from D6-19; and 1 antibody from DK4; all of which bind to PDGFD. Five antibodies are provided that are

encoded by or derived from JH4b; 1 antibody from JH5b; and 13 antibodies from JH6b, all of which bind to PDGFD. One of skill in the art, provided with the teachings of the present specification would not find determining which V D J sequences to combine to make antibodies binding to PDGFD unpredictable but fully enabled.

With regard to written description, Applicants respectfully submit that specification unquestionably
provides written description as to the structure of the light chain. The specification specifically provides: 1) light chain germline sequences (see page 62, lines 18-2 and page 64, lines 1-24); 2) specific light chain sequences (Figures 3-21, nucleic acid sequences SEQ ID NOs: 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 81, 83, 85, 87, 89, 91, amino acid sequence SEQ m NOs:14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 39, 41, 43, 45, 47, 49 and Figure 49); and 3) specific light chain CDR sequences for a human monoclonal antibody that binds to PDGFD (see Figure 49). Applicants have specifically provided written description that VH1-8 delived sequences can be combined with sequences derived from light chain sequences A19 (Antibody 1.49); A20 (Antibody 1.45); A27 (Antibody 6.4); and A30 (antibodies 1.19, 1. 18 and 1.46) to obtain antibodies specific for PDGFD. More specifically, for example, Applicants described one possible light chain that can be paired with the heavy chain of SEQ ID NO: 48 is light chain SEQ ID NO: 49, see Example 7 beginning at page 56, Figure 21. The present specification contains written description of 19 specific physical embodiments of a human monoclonal antibody that binds to PDGFD.

In response to applicant's agruement that any combination of heavy and light chain for antibody in claim 1 is enabled, claim 1 still recites a human monoclonal antibody that binds to Platelet Derived Growth Factor (PDGFD) and comprises a heavy chain acid sequence comprising SEQ ID NO: 48. However, the monoclonal antibody in claim 1 is missing the the amino acid squence of the light chain. The specification as filed does not teach any combination of heavy and light chain woud produce antibody that maitains its binding specificity to PDGFD. The specification teaches the specific monoclonal antibody that binds to PDGFD comprising the specific combination of heavy and light chain amino acid squences. Amending claim 1 to include the amino acid sequence of the ligth chain would obviate the enablement and written description rejections.

In response to applicant's agruement that V D J genes for antibodies specific for PDGFD are enabled, the scope of claim 22 encompasses any human monoclonal antibody or antigen binding portin thereof that binds to PDGFD and is encoded by any human "V_H1-8 gene" and "J_H6B gene". However,

the polynucleotide sequences of "V_H1-8 gene" and "J_H6B gene" that encodes the claimed human monoclonal antibody to PDGFD are not recited in the claim. Amending claim 22 to recite the specific polynucleotide sequences of the heavy and light chain that encode the claimed monoclonal antibody would obviate the enablement and written description rejections. With regard to dependent claim 24, the claim encompasses any CDR2, and any CDR3 region of heavy chain and any CDR1, any CDR2 and any CDR3 regions from any light chain so long the antibody has heavy chain CDR1 from residues 26-35 of SEQ ID NO: 48. There is insufficient guiance as to the amino acid residues of the CDR2, and CDR3 region of heavy chain and any CDR1, CDR2 and CDR3 regions from light chain for the claimed antibody. The same reasonings apply to claims 24-32, 34-43 and 45. Amending the claims to recite the specific combination of CDR1, CDR2, and CDR3 of heavy and light chain will obviate the enablemenent and written description rejections. Applicant is remined that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). See MPEP 2145.

Claims 22, 30-32, 40-43 and 45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 6,706,687 (March 16, 2004; PTO 892) in view of Green et al (Nature Genetics 7: 13-21, May 4, 1994; PTO 892).

Applicants' arguments filed 5/4/05 have been fully considered but are not found persuasive. Applicants' position is that the method taught by Green et al did not teach or suggest a human monoclonal antibody derived from VH1-8 and furthermore from D5-18 which would have specificity to PDGFD. It could not have been known to specifically use VH1-8, VH6B and furthermore D5-18 to provide a human antibody that binds to PDGFD.

In response, the reference human antibody appears have the same binding specificity as the claimed antibody and it obviously derived from the same human genes such as VH1-8 and D5-18 or D5-18. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). All rejections remain.

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600